

REMARKS

Claims 1, 3-43, and 45-54 are pending in the application after entry of this amendment. Claims 1, 3-43 and 45-50 stand rejected. Claims 4, and 43 have been amended. Claims 51-54 are newly added.

Rejections under 35 USC §103

Claims 1-3, 6-12, 19-22, 30, 32-25, 42-46, and 48-50 were rejected under 35 USC § 103(a) as being unpatentable over US 2004/0121336 to **Greenfield *et al.*** as evidenced by **Ishikawa *et al.*** in view of US 6,060,246 to **Summerton**. This rejection is traversed. The claims, as presently amended, relate to the isolation of nucleic acids with a cleavable solid phase for binding nucleic acids having the claimed onium groups. The combined teachings of Greenfield and Summerton do not teach or suggest the presently claimed method of isolating nucleic acids using a nucleic acid binding solid phase wherein the nucleic acid binding portion includes a ternary or quaternary onium group wherein all R groups have from 4-20 carbon atoms, as called for in claim 3. The sole quaternary onium groups identified in Summerton are quaternary ammonium groups identified as DEAE and QAE. Neither of these groups have 4 or more carbons for any of the groups on the nitrogen. Neither group teaches the desirability of such substitution. The recitation of various quaternary ammonium groups in paragraph 1 of the Office Action that Greenfield allegedly discloses as nucleic acid binding groups is actually a listing of cations that can be added to binding solutions. It is not a listing of contemplated nucleic acid binding groups. There is no teaching in either reference of quaternary ammonium groups wherein all R groups have from 4-20 carbon atoms or of any quaternary phosphonium or ternary

sulfonium groups. As the references fail to teach all elements of the claims no *prima facie* case of obviousness can be established based on this combination.

Regarding claims 48 and 50 and as it might apply to new claim 54, the passage in Summerton cited by the Examiner (col. 14, lines 16-24) describes amplification of nucleic acid on a solid phase and not a solution containing the released nucleic acids as recited in the claims. It is further pointed out that the presently claimed method, using the solution resulting from cleaving the bound nucleic acids, necessarily means that the amplification solution also contains the cleaved fragments from the binding material, i.e. linker fragment and onium group as well as the excess cleavage reagent. This is particularly the case when the cleavage reagent is an excess of a strongly alkaline solution. Any of these might have been reasonably expected by one of skill in the art to have an inhibitory effect on the downstream process. It was not obvious until Applicants' successful demonstration that this method would work. That one of skill in the art would not have considered it obvious to use such a solution in a downstream amplification reaction is witnessed by the many isolation procedures known in the art that require scrupulous purification of isolated nucleic acid before amplification.

Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

Claims 3-5 and 47 were rejected under 35 USC § 103(a) as being unpatentable over US 2004/0121336 to **Greenfield *et al.*** as evidenced by **Ishikawa *et al.*** in view of US 6,060,246 to **Summerton** and further in view of US 6,602,657 to **Bronstein *et al.*** and further in view of US 6,818,454 to **Goshe *et al.*** This rejection is traversed. As noted

above the combination of Greenfield and Summerton does not disclose or suggest C₄-C₂₀ quaternary ammonium groups or C₁-C₂₀ quaternary phosphonium groups. Bronstein and Goshe are cited to support a finding that all quaternary ammonium, phosphonium and sulfonium groups are equivalent in distant unrelated fields and when combined with Greenfield and Summerton render obvious the use of the presently claimed materials having C₄-C₂₀ quaternary ammonium or C₁-C₂₀ quaternary phosphonium binding groups because all have a permanent positive charge. Applicants point out however that the attraction of nucleic acids with having small, 1-2 carbon groups has been known for at least 15 years before their invention tracing back to at least the disclosure of EP 0496822A1, cited in the specification. However no reports of which Applicants are aware exist showing the use of larger quaternary ammonium groups, any quaternary phosphonium groups, or ternary sulfonium groups for this purpose prior to their invention. The tenacity or strength with which the materials of the present claims bind nucleic acids exceeds that of materials with conventional lower (C₁ – C₂) alkyl groups known in the art. It is because of this exceptional strength that the present materials resisted removal with numerous known eluent compositions, as described at page 14, line 30 to page 15, line 16, and the cleavage method was devised. Applicants maintain that the art cited does not demonstrate equivalence of all ammonium, phosphonium and sulfonium groups and does not establish *prima facie* obviousness.

Claims 13-15 and 23-29 were rejected under 35 USC § 103(a) as being unpatentable over US 2004/0121336 to **Greenfield *et al.*** as evidenced by **Ishikawa *et al.*** in view of US 6,060,246 to **Summerton** and further in view of US 5,707,559 to **Schaap**

et al. This rejection is traversed. As noted above the combination of Greenfield and Summerton does not disclose or suggest C₄-C₂₀ quaternary ammonium groups or C₁-C₂₀ quaternary phosphonium groups. Schaap is cited for its teaching of cleavable dioxetanes and alkenes convertible to cleavable dioxetanes. The Examiner alleges that

“Luminescence upon cleavage would have provided an additional method of detecting cleavage of the non-specifically bound nucleic acids from the capture agent, and would have provided an additional method for detection and analysis of the released nucleic acids”.

The Schaap reference does not teach any example of use of dioxetanes or electron-rich alkenes as linkers or any examples where such a molecule could be linked at two distinct sites to two different species as is required. Nor does it teach how such a compound could be made. Thus Schaap is defective as a reference on at least this ground. Moreover Applicants assert that the alleged motivation for combining Schaap with Greenfield and Summerton recited above would be not be obvious to one of skill in the art. It can be readily seen that the luminescent cleavage alleged to indicate cleavage of non-specifically bound nucleic acids in fact only would indicate cleavage of linker. It would not give any indication of whether any nucleic acid had been first bound and then later released since signal would always be generated upon cleavage of linker. As such it would be unreliable as an indicator of nucleic acid release or as an analysis tool. Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

Claims 16 and 17 were rejected under 35 USC § 103(a) as being unpatentable over US 2004/0121336 to **Greenfield et al.** as evidenced by **Ishikawa et al.** in view of US

6,060,246 to **Summerton** and further in view of US 6,514,700 to **Singh et al.** This rejection is traversed for the reasons stated above in connection with the rejection of claims 1-3, 6-12, 19-22, 30, 32-25, 42-46, and 48-50. Applicants maintain that Greenfield in combination with Summerton do not render any claim obvious as the combination does not teach or suggest the claimed nucleic acid binding groups and that the additional citation of Singh does not cure this defect. Since no *prima facie* case of obviousness has been established, withdrawal of the rejection is respectfully requested.

Claims 36-37 and 41 were rejected under 35 USC § 103(a) as being unpatentable over US 2004/0121336 to **Greenfield et al.** as evidenced by **Ishikawa et al.** in view of US 6,060,246 to **Summerton** and further in view of **Mukhamedgaliev** and further in view of **Reinecke** and further in view of **Bronstein et al.**, and **Goshe et al.** This rejection is traversed. This rejection is traversed for the reasons stated above in connection with the rejection of claims 1-3, 6-12, 19-22, 30, 32-25, 42-46, and 48-50. Applicants maintain that Greenfield in combination with Summerton does not render any claim obvious as the combination does not teach or suggest the claimed nucleic acid binding groups and that the additional citation of the additional references does not cure this defect. Since no *prima facie* case of obviousness has been established, withdrawal of the rejection is respectfully requested.

Request for English Translation of Russian Reference

Applicants again note that the rejection relies on Mukhamedgaliev et al, which is in Russian and not English. Applicants maintain that a reference is prior art for all that it

teaches. Beckman Instruments v LKB, Produkter A.B., 892 F. 2d 1547, 1551 (Fed. Cir. 1989). It is inappropriate to base a rejection of a patent claim based on only selective portions of a reference, in this case the English language abstract, ignoring other portions. With respect to reliance on foreign language documents in support of a rejection, MPEP 706.02 states:

... If the document is in a language other than English and the examiner seeks to rely on that document, a translation must be obtained so that the record is clear as to the precise facts the examiner is relying on in support of the rejection. The record must also be clear as to whether the examiner is relying upon the abstract or the full text document in support of a rejection. The rationale for this is several fold. It is not uncommon for the full text document to reveal the document fully anticipates an invention that the abstract renders obvious at best. *The converse may also be true, that the full text document will include teachings away from the invention that will preclude an obviousness rejection under 35 U.S.C. 103, when the abstract alone appears to support the rejection.* ... (Emphasis added)

Absent the ability to know all of what Mukhamedgaliev teaches, not limited to the abstract and drawings, Applicants are prevented from the opportunity to rebut the Examiner's interpretation. Applicants respectfully request the Examiner to obtain a translation of Mukhamedgaliev et al from the Translations Branch of the Scientific and Technical Information Center (STIC) in accordance with MPEP 901.05(d) and provide Applicants with a copy of the same. Further, Applicants maintain that serious questions remain regarding what is actually disclosed in Mukhamedgaliev et al. According to MPEP 706.02(j), a rejection under 35 U.S.C. 103 should include a recitation of the differences in the claim over the applied references. As such, the Examiner cannot discharge her duties without obtaining an English translation of Mukhamedgaliev et al. and identifying the differences between the claims and the reference, and allowing

Applicants to respond to such a rejection with the English translation in hand. Applicants maintain that in the absence of being supplied with a copy of an English translation of Mukhamedgaliev et al, no *prima facie* case of obviousness has been established, and withdrawal of the rejection is respectfully requested.

Claims 38-40 were rejected under 35 USC § 103(a) US 2004/0121336 to **Greenfield et al.** as evidenced by **Ishikawa et al.** in view of US 6,060,246 to **Summerton** in view of US 3,855,310 to **Hughes** (1996 Tetrahedron Letters 37(42): 7595-7598) and further in view of US 4,904,819 to **Hagashita**. This rejection is traversed for the reasons stated above in connection with the rejection of claims 1-3, 6-12, 19-22, 30, 32-25, 42-46, and 48-50. Applicants maintain that Greenfield in combination with Summerton do not render any claim obvious and that the additional citation of Hughes and Hagashita does not cure this defect.

Moreover, neither Hughes or Hagashita disclose any triphenylphosphine containing compounds attached to a resin, nor does either reference disclose the use of any triphenylphosphine containing compounds in a Wittig reaction where the phosphorus-containing group would be cleaved from a resin. Different chemical reactions are disclosed in Hughes for performing this cleavage. Examples include a Wittig reaction and a hydrolysis reaction. In all examples the phosphorus remains attached to the bead and may in some cases be converted to a phosphine oxide moiety in the process of the cleavage reaction. These reactions are distinct from what is in operation in the claimed methods. Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

All grounds for rejection having been addressed, and to the best of Applicants' knowledge overcome, Notice of Allowance is respectfully requested.

/Richard S. Handley, Ph.D. Reg. No. 38,484/

Richard S. Handley, Ph.D.

Reg. No. 38,484